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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/738,066 12/15/00 NUSS

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HM22/1010

EXAMINER

UPPJ,R

ART UNIT

PAPER NUMBER

1624

DATE MAILED:

10/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/738,066

Applicant(s)

NUSS ET AL.

Examiner

Rao M Uppu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 December 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-78 is/are pending in the application.
- 4a) Of the above claim(s) 75 and 76 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-74, 77 and 78 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I Claims 1-74, 77 and 78, drawn to compounds of formula (I) where $n=0$,¹
W=N and Z=N, their pharmaceutical composition(s) and methods of use,
classified in classes/subclasses 514/258 and 544/279.
- II Claims 1-74, 77 and 78, drawn to all other compounds of formula (I) NOT
provided for by group I, their pharmaceutical composition(s) and methods
of use, classified in classes 514, 540, 544 and 546, subclasses depend on
the nature of heterobicyclic core and the choice of substituents R_1-R_6 and
 $R'_1-R'_4$.
- III. Claims 75 and 76, drawn to methods of employing compounds of group I
in combination with other active ingredients (e.g., insulin, troglitazone,
rosiglitazone, pioglitazone, glipizide, and metformin).
- IV. Claims 75 and 76, drawn to methods of employing compounds of group II
in combination with other active ingredients (e.g., insulin, troglitazone,
rosiglitazone, pioglitazone, glipizide, and metformin).

If group II is elected, applicants must further (1) pick compounds of one specific heterobicyclic core defining precisely the variables W, Z and n, (2) elect a single disclosed species that belongs to that core, and (3) indicate which claims read on the elected species.

The inventions are distinct, each from the other because of the following reasons:

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Compounds of group I are substituted pyrido [4,3-d] pyrimidines, whereas Group II embraces compounds having multiple heterobicyclic cores. The two groups, which have structurally dissimilar cores, were made independently and used independently. They would be expected to raise different issues of patent ability if a compound of group I was anticipated; the anticipatory reference would not necessarily render obvious the other group II or vice-versa. They are not art recognized equivalents, as they are classified diversely from classes/subclasses, and require separate literature searches. Groups II and III are independent and distinct because the uses recited for compounds of group III may be old or obvious when employing the active ingredient(s) of group I but may be patentable due to superior or synergistic properties not present in the individual compounds of group I. Similarly, groups II and IV are independent and distinct because the use recited for compounds of group IV may be old or obvious when employing the active ingredient(s) of group I but may be patentable due to superior or synergistic properties not present in the individual compounds of group II. Finally, groups III and IV are independent and distinct because they embrace compounds of structurally dissimilar cores (i.e., groups I and II, respectively). The multiple combinations as recited within groups III and IV require independent searches and thus have acquired a separate status in the art.

Should Applicants traverse on the grounds that the species are not patentably distinct, Applicants should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over

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the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicants are advised that the reply to this requirement to be complete must include an election of the group (I, II, III, or IV) to be examined even though the requirement is traversed (37 CFR 1.143).

During a telephone conversation with applicants' attorney Mr. David Lentini on September 14, 2001 a provisional election was made with right of traverse to prosecute group I, claims 1-74, 77 and 78 (i.e., compounds of formula (I) in which $n=0$, $W=N$, and $Z=N$). Applicants must make affirmation of this election in replying to this Office action. Claims 75 and 76, together with the non-elected subject matter in claims 1-74, 77 and 78, are withdrawn from further consideration by the Examiner, 37 CFR 1,142(b), as being drawn to a non-elected group.

Applicants are reminded that upon the cancellation of claims to a non-elected Group(s), the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

When a non-provisional application is entitled to an earlier U.S. effective filing date of one or more provisional applications under 35 USC 119(e), a statement such as,

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"This application claims the benefit of U.S. Provisional Application No. 60/172,403, filed 12/17/2000" should appear as the first sentence of the specification.

The sentence, "The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows" that precedes the phrase "That which is claimed:" on page 47 superfluous. Applicants' are requested to delete the sentence.

Claim Objections

Claim 77 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1, the only difference being the intended use which is not given material weight. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112 (Second Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-74, 77 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i). Claims 1-34, 69, 70, 71-74 are rejected because the phrase "a compound having the structure" recited in claim 1 is open-ended. One skilled in the art does not know what

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other structures are embraced by the claim language other than the structure shown in (I). Correction of the phrase to "a compound of structure (I)" or "a compound of formula (I)" is suggested.

ii). Claims 35-68 are rejected because the phrase "a compound having the structure" recited in claim 35 is open-ended. One skilled in the art does not know what other structures are embraced by the claim language other than the structure shown in (I). Correction of the phrase to "a compound of structure (I)" or "a compound of formula (I)" is suggested.

iii). The phrase "a composition" recited in claim 69 makes claims 69, 70, 72-74 indefinite. It is not clear what composition the applicants are referring to. If applicants' intended meaning is pharmaceutical composition, a correction of the phrase to "a pharmaceutical composition" is suggested to overcome this rejection.

iv). The meaning of the terms "loweralkylcarbonyl" and "lowerheteroarylcarbonyl" recited in claims 12, 13, 46, and 47 is not clear. The specification on pages 16-22 does not provide any guidance as to which compounds are embraced by the instant claims. Clarification is requested.

v). Claim 78 is rejected because the instant claim provides for the use of a compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/ process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

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Claim 78 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131,149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-74, 77 and 78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

i). Claims 1-34, 69, 70, 71-74 are rejected because, in claim 1, X and Y are defined as independently selected from the group consisting of nitrogen, oxygen, and optionally substituted carbon. The claim 1 also recites that X and Y have two substituents each (R_1 and R'_1 in the case of X; and R_4 and R'_4 in the case of Y) (see structural formula (I) on page 47). The said substitutions are possible if only oxygen and nitrogen are tetravalent, and carbon is pentavalent. (Note that the definitions of X and Y include optionally substituted carbon and not just the elemental carbon). Compounds having tetravalent oxygen and pentavalent carbon have never been disclosed in the chemistry

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literature. Nitrogen can be tetravalent but the compound made should be an ion and positively charged, for which the specification does not provide enablement.

ii). Claims 35-68 are rejected because, in claim 35, X and Y are defined as independently selected from the group consisting of nitrogen, oxygen, and optionally substituted carbon. The claim 35 also recites that X and Y have two substituents each (R_1 and R'_1 in the case of X; and R_4 and R'_4 in the case of Y) (see structural formula (I) on page 52). The said substitutions are possible if only oxygen and nitrogen are tetravalent, and carbon is pentavalent. (Note that the definitions of X and Y include optionally substituted carbon and not just the elemental carbon). Compounds having tetravalent oxygen and pentavalent carbon have never been disclosed in the chemistry literature. Nitrogen can be tetravalent but the compound made should be an ion and positively charged, for which the specification does not provide enablement.

iii). Scope of Enablement: Claims 72-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of GSK3, does not reasonably provide enablement for treatment GSK3-mediated disorders generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The compounds of the instant application are taught as inhibitors of GSK3 and at best would be useful in treating disorders that involve excessive expression GSK3. The disorders mediated by GSK3, on other hand, would include disorders of higher as well as lowered expression of GSK3. Therefore, the

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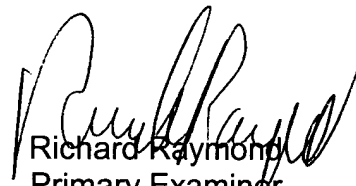
diseases recited in the instant claims are not of the same scope as the ones generically embraced by the instant specification.

Any inquiry concerning this communication from the examiner should be directed to Rao M. Uppu whose telephone number is (703) 308-3951. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund J. Shah, can be reached on (703) 308-4716. The fax number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or Proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Rao M. Uppu, Ph.D.
Examiner
Art Unit 1624


Richard Raymond
Primary Examiner
Art Unit 1624